Iron deficiency in Bangladeshi women and the available treatment options to recover it

By

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A thesis submitted to the Department of Pharmacy in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy (Hons.)

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Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

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Ethics Statement

This study does not involve any human and animal trial.

Abstract

Iron deficiency anemia (IDA) is the most common nutritional problem globally including Bangladesh and it poses a public health challenge. According to the World Health Organization (WHO), approximately one third of the world population is suffering from iron deficiency and IDA affects over 1.2 billion people worldwide. Iron deficiency is found to be prevalent in 41.8 percent of the female population in Bangladesh. The risk of iron deficiency is especially high among women of reproductive age and premenopausal women. Pre-mature child birth, increased neonatal mortality, maternal death, poor brain performance, depression etc. are linked to iron deficiency. However, iron deficiency can be screened using hemoglobin concentration, while it can be confirmed by using serum ferritin concentration. Iron supplements (oral and intravenous dosage forms) can combat iron deficiency and cure it. This study aims to review the iron deficiency status of Bangladeshi women and to identify the best viable treatment options.

Keywords: Iron deficiency; Anemia; Bangladeshi Women; Ferritin; Hemoglobin.

Dedication

This work has been dedicated to my parents for their support and my teachers for their proper guidelines.

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Contents

List of figures

List of tables

List of Acronyms

IDA	Iron deficiency anemia
FDA	Food and Drug Administration
Hb	Hemoglobin
Hct	Hematocrit
FCM	Ferric carboxymaltose
ESAs	Erythropoiesis stimulating agents
TSAT	Transferrin saturation
IPC	Iron polymerase complex
IG	Iron gluconate
CMS	The Centers for Medicare and Medicaid Services
WHO	World Health Organization
CRF	Chronic renal failure
CKD	Chronic kidney disease
NPNL	Nonpregnant and nonlactating

BDHS	Bangladesh Demographic and Health Survey
GIT	Gastro-intestinal tract

Chapter 1: Introduction

1.1 Pivotal role of iron in the body

Iron is an important nutritional material that serves a variety of roles in our bodies. These roles involve maintaining energy output in our cells and generating essential hormones and neurotransmitters in the brain. Iron is also essential for collagen formation, and thus for the ongoing regeneration of bones, cartilage, and connective tissue. However, the rest of the iron in our bodies is used to produce blood, or perhaps more accurately, red blood cells and the blood protein hemoglobin. A red blood cell has a lifespan of around 120 days, which ensures fresh hemoglobin must be created on a regular basis. Iron is also required for the transport of oxygen in our muscles, specifically for the development of myoglobin, a transport protein. If anyone doesn't have enough iron, she/he won't be able to complete this mission, and the body's oxygen transport will decline. Human cells, tissues, and organs aren't getting sufficient oxygen from the lungs, and the whole body isn't "firing on all cylinders" to any degree (Abu- Ouf & Jan, 2015).

1.2 Iron deficiency and it's root causes in women

Iron deficiency (ID) is the most common nutritional problem globally and poses a public health challenge. Despite iron being one of the most abundant elements in the earth's crust, prevalence of ID is quite common in women across the world. According to the World Health Organization (WHO), approximately one third of the world population is suffering from ID which in turns causing anemia. It has been reported that ID affects women and children incommensurately. Different phases of ID include mild deficiency, marginal deficiency and iron deficiency anemia. Mild deficiency is characterized by depleted iron stores, marginal deficiency is marked by compromised production of iron-dependent proteins and ID anemia is identified by insufficient hemoglobin synthesis and reduced oxygen transport to the tissues (Coad & Pedley, 2014) .

The world's most prevalent deficiency in micronutrients is Iron Deficiency, with > 20% of women reproducing. It is a major issue of global public health that influences mortality among mothers and children, physical fitness and health professionals. Children aged 0 to 5 years, women, and pregnant women are particularly vulnerable. Chronic diseases, particularly chronic kidney disease, chronic cardiac failure, cancer and inflammatory bowel disease are sometimes linked to iron deficiency anemia. Treatment methods include prevention, including dietary fortification and iron supplements, in addition to research and treatment on the origin of iron deficiency iron. Oral iron is commonly prescribed as a first-line treatment, but the most recent intravenous iron formulations, available almost a decade ago, appear to replenish iron stocks easily and efficiently (Lopez et al., 2016).

When there is a very low absorption of iron in the body it causes iron deficiency. Additionally, iron deficiency occurs when the body receives insufficient amounts of iron and losses significant amounts of blood from the body can also cause iron deficiency. There are a number of medical conditions that might result in iron deficiency. Medications used to treat renal diseases and inflammation caused by congestive heart failure may cause iron deficiency. In the developing and under-developing countries, the women have iron deficiency because of hunger, poverty and bad diet plan. But women from developed countries don’t face iron deficiency because they are not facing these problems. They might face it because of menstruation, donation of blood and less amount intake of iron. Those women who usually don’t eat meat or who are vegetarian they need to increase taking iron to 18 to 32 milligram per day (Coad & Conlon, 2011a). Pregnancy is one of the most important reasons of causing iron deficiency in women. It results in loses of 1.2 gm iron during pregnancy. The amount of iron loses of Fetus, placenta, erythrocyte expansion and basal are respectively 270 mg, 90 mg, 450 mg and 230 mg (Gambling et al., 2011). In older patient, blood loses because of different type of cancer, using of non-steroidal anti-inflammatory drugs (e.g. aspirin), decreased ability of producing gastric acid can cause iron deficiency (Goddard et al., 2011).

Table 1: Common causes of iron deficiency.

Causes	Example
Physiological	Prematurity, growth spurt and pregnancy
Bad dietary plan	Malnutrition, pseudo-bulbar palsy, vegans, chronic illness and poor socio-economic state
Malabsorption	Celiac disease and atrophic gastritis
Blood loss	Esophageal varices, hiatus hernia, gastritis, peptic ulcer, inflammatory bowel disease, hook worm, hemorrhoids and menorrhagia

It is essential that humans have iron in their bodies as an element. The sources of iron include different elements like, iron-rich foods, taking supplements or receiving transfusions. Iron deficiency may have many causes. If we can figure out the source of iron deficiency, it will make things lot easier for us in treating it. In order to identify whether there is a shortage of iron in the human body, a blood test is the most accurate. The first and foremost thing should be done by the iron deficient is to find what is the reason of getting iron deficiency and what can be done to cure it before it becoming serious for health. There are some types of people who need iron more especially, children, old people, breast feeding mothers, athletes etc. Children who don't get enough iron during their childhood they face different situation like slow language acquiring, bad memory, become less attentive and ultimately fall behind in school (Story et al., 2010).

ID is a medical term that refers to a lack of iron when serum ferritin levels fall underneath 20–30 g/L, it is classified as severe iron deficiency, and when serum ferritin levels fall below 70–100 g/L, it is classified as gentle iron deficiency. The ferritin level is used as a surrogate marker for determining the identity of a person. Because serum ferritin is an acute phase reactant that can be elevated in case scenarios of inflammation or infection, a concurrent test for inflammatory markers is recommended in cases of anemia with elevated ferritin to rule out reactive causes. If the ferritin amount is higher than 100 g/L, ID indicates the absence of anemia (Khalafallah & Dennis, 2012).

1.3 Signs and symptoms of Iron Deficiency

There are a number of signs and symptoms for iron deficiency. Faint skin is one of the signs of iron deficiency. The skin of a person who has iron deficiency will be looked pale. Some damage in nails will indicate the lacking of iron in body. Additionally, swelling in tongue and cracks in mouth indicates iron deficiency. Various Symptoms will also start to show as soon as iron deficiency occurs; such as, pain in the chest and dizziness. Additionally, hands and feet will start to become cold and there will be some difficulty in giving concentration. Furthermore, there will be fatigue or tiredness whole day which is the most common symptom of iron deficiency. Irregular heartbeat also indicates serious type of iron deficiency. Headache and breathing problem also can be shown as the symptom of iron deficiency. In addition to that, some people have very low iron concentration in their body without showing any serious signs and symptoms.

Therefore, people should be more focused on their daily intake of iron in their body before being diagnosed with iron deficiency as it can be dangerous for them (C & WA, 2010).

1.4 Types of anemia

Iron deficiency anemia: This type of anemia occurs due to iron deficiency in the body. It is the most common type of anemia. Girls who go with menstruation and result in excessive blood loss, pregnant women and children face this more frequently. Iron supplement and treatment based on the cause can be main treatment for this type of anemia (Toxqui & Vaquero, 2015) .

Thalassaemia: Thalassaemiais a condition which affects levels ofhemoglobin in the body. Thalassaemia patients produce a very little or no amount of hemoglobin in the body (Locatelli et al., 2016).

Aplastic anemia: Aplastic anemia is caused by the damaged bone marrows and these bone marrows are unable to produce red blood cells in the body (Young et al., 2008).

Hemolytic anemia: It can be caused by some acquired diseases. Different types of acquired diseases result in making incomplete or deformed red blood cells. These deformed red blood cells die quickly and cause hemolytic anemia (IA, 1992).

Sickle cell anemia: If the red blood cells are sickle shaped and function less then, it can be said that, there is sickle cell anemia in that person's body. In this type of anemia less amount of healthy red blood cells present and they are mostly unable to carry oxygen in the body (Steinberg, 2008).

Pernicious anemia: It is a one type of anemia when there is an inability of intestine to absorb vitamin B12 which results in decrease of red blood cells (Semba et al., 2013).

Fanconi anemia: The failure in the bone marrow results in decreased production of different types of blood cell, thus, cause fanconi anemia (Wang, 2016).

1.5 Consequences of iron deficiency in neonatal and postnatal development

In all the stages of iron deficiency people start to get poorer brain performance. The brain doesn't work normally when the body is iron deficient. There will obviously some different behavioral changes to the neonatal iron deficient and postnatal iron deficient. In neonatal ID, the iron supply decreases and the demands has increased by the mother's gestational condition. Placental nutrient flow has been hampered and often causes premature birth because of mother's IDA or maternal hypertension (Georgieff, 2011). Studies have been conducted on neonatal iron deficiency's impact on behavior in people and lab animals. Iron deficiency has been linked to reduced cognition and attention, which is characterized by inactivity, impatience and drowsiness, loss of focus, anxiousness, hypoactivity, and lack of energy. Additionally, postnatal iron deficiency is thought to induce delays in social and emotional behavior, as well as physical and mental development (Georgieff, 2011).

1.6 Complications of iron deficiency

Different types of complications can be found due to iron deficiency. If iron deficiency is undiagnosed and untreated it may show a lot of complications in human body. Among them, depression starts to show in very early phase and lifestyle has been hampered. Depression can make anyone mentally weak which will lead them to a worst condition. Additionally, several heart problems can occur because of iron deficiency. Usually, hemoglobin in red blood cell carries oxygen to the lungs and passes it to the body's all tissues. If the body doesn't have proper red blood cells which are carrying hemoglobin, heart has to work hard to distribute oxygen rich blood in the body. Cells need oxygen to function well. As there is iron deficiency in the body, heart has to function a lot which can lead different problems like irregular heartbeat, heart damage even heart failure can be occurs. Moreover, the risk of getting infected increases as hemoglobin in red blood can't function properly. The children with iron deficiency don't have proper development in their body. Moreover, pregnant women give premature birth or a very low weight birth of children. Iron deficiency also weakens our immune system which make people susceptible to flu, cold and different types of infections. Although many people do not have complications in their body because of iron deficiency everyone needs to be serious on iron deficiency and its complications. Anemia caused by iron deficiency compromises the immune system, making people more vulnerable to infections, and impairs the body's capacity to fight infections (Sutherland et al., 2018)

1.7 Rationale of the study

Iron is a very important element for our body because it helps to maintain a lot of function in the body. Hemoglobin, a part of red blood cells which carries oxygen to the blood has been produced by iron. Iron is also important for good skin, nice hair, nice nails and healthy cells. Very less amount of iron than the required in our body causes iron deficiency. In Bangladesh, women from rural area and even from city area have iron deficiency. It is a very common problem for the women in Bangladesh. Iron deficiency is an alarming problem for most of the women. This review is to get a comprehensive idea of iron deficiency in women and provide an overview on iron deficiency in Bangladeshi women and the treatment option available to cure it. According to the World Health Organization, iron deficiency anemia affects over 1.2 billion people, and iron deficiency without anemia is more common. IDA is the most prevalent micronutrient disease, impacting millions of men, women, and children in their health and socio-economic well-being (Baltussen et al., 2004).

The risk of premature delivery and low birth weight is significantly increased by maternal anemia, and 115,000 maternal deaths and 591,000 perinatal deaths per year are caused by iron-deficiency anemia. From the researchers, Roughly 45% of women in Bangladesh have prevalence of anemia; however, it is unknown how many of them have iron deficiency anemia and how many have iron depletion, due to the lack of available data though it can be assumed that, the number is high. The truth is that internationally, it is estimated that 50% of all anemia is due to iron deficiency. Globally, iron deficiency is the 9th most significant risk factor, killing 841,000 people and depriving 35,057,000 people of quality of life. The 14th most prevalent disease burden is that of iron deficiency anemia (Murray & Lopez, 1996).

IDA is considered to be a serious public health concern, and as such, governments, researchers, and healthcare practitioners must work together to tackle it (McLean et al., 2008). Iron deficiency anemia is caused by a long-term iron imbalance, resulting in reduced or exhausted iron reserves (Allen, 2000; Clark, 2008; Ramakrishnan & Yip, 2002).Disastrous consequences include growth retardation, cognitive limitations, low work ability, and overall diminished quality of life (Macdougall et al., 1975; Newhouse et al., 1989; Preziosi et al., 1997; Soewondo et al., 1989; Walter et al., 1989; Zhu & Haas, 1997).These consequences arise with so many problems for people in this world as well as in Bangladesh. So finding the best treatment options and studying the overall scenario of iron deficiency in Bangladeshi women can bring some light in this case, which is the main rationale for this study.

1.8 Aim and objectives of the study

The aim is to discuss the current scenario of iron deficiency in Bangladeshi women and how can this be treated to overcome this situation and providing a narrative assessment of recent researches on the routine usage of iron complement alternatives to treat IDs, including oral and intravenous iron (IV) formulations with an emphasis on safety issues.

Objectives of the study:

- Describing the overall scenario of iron deficiency in Bangladeshi women.
- Delineating the consequences of iron deficiency in Bangladeshi women.
- Finding the best way to evaluate iron status.
- Focusing on the available treatment option to treat IDA.
- Explaining the dietary skills, attitude and practices of women in IDA.

Chapter 2: Methodology

This review paper was written using information gathered by searching scientific journal papers and finding pertinent information. This project paper has used evidence, data, and statistical values taken from different academic sources such as books, conference proceedings, and research papers. The material was extracted, integrated, and synchronized after performing a thorough examination of a variety of studies. Selection and examination of relevant content resulted in the extraction of key information. The following best information, according to the topic, was then found that fits well with the topic. The following online resources and search engines have been utilized to find relevant materials as needed: Google scholar, PubMed, Medline, Science Direct, Elsevier, Springer and Nature.

Chapter 3: An overview on iron deficiency in Bangladeshi women

3.1 Iron deficiency in urban adolescence (college and school girls) of Bangladesh

Most of the women in our country have iron deficiency in common, where a large number of those deficient are girls from schools and colleges in urban areas. More than 1 billion people are suffering from iron deficiency worldwide. Iron deficiency was found to be prevalent in 41.8 percent of the women's population in Bangladesh. In addition to iron deficiency, deficits of folic acid, vitamin B12, and vitamin A can also be essential causes of nutritional anemia. Non-nutritive causes of anemia, such as hemorrhage, infection, and genetic defects, can also play a significant role (Ahmed et al., 2000). Girls at the age of 10-20 years are at high risk for anemia. These girls are likely to become pregnant, their development during puberty would have an effect on their capacity to bear a healthy baby, and hence decide the well-being of the next generation. These young women are mainly from modestly educated families who resided in a peri-urban environment with a low to moderate socioeconomic status. Girls who attend school are more likely to come from families of higher educational levels, as shown by socioeconomic statistics (Ahmed et al., 2000). The girls' with ID are found to show dietary patterns of very low intakes of eggs, milk, and meat, as well as a very low dietary intake of variety of essential micronutrients and protein. It indicates that 25% of the girls did not consume big fish at all, and another 36% consumed them only rarely, suggesting a possible protein deficiency. The current study's findings have significant repercussions for iron supplementation programs (Ahmed et al., 2000). A huge number of teenage girls in Bangladesh suffer from different forms of malnutrition. Poor dietary status in adolescence is a significant predictor of health outcomes later in life. As a result, teen wellbeing and wellness should be prioritized. In the last few years, a few studies have been conducted in Bangladesh to determine the degree and consequences of malnutrition in rural and urban teenage school girls, as well as adolescent female staff. Findings of these experiments support the higher incidence of anemia, iron deficiency, and other micronutrient deficiencies. The overall nutritional condition of Bangladeshi urban teen college girls is deplorable. The prevalence of anemia, as well as awareness of anemia and iron-rich diets, is insufficient among college girls in this sample. As a result, appropriate steps to boost their nutritional status and reduce the incidence of anemia should be taken (Kabir et al., 2010). The findings of different studies show that, adolescent school girl are at higher risk of anemia and iron deficiency. It is so much necessary to educate them about this issue and we should encourage them to intake sufficient amount of iron, vitamin A, vitamin B12, folic acid which can be found from different types of foods and supplements. The girls from urban area need extra importance as there is a little opportunity of them to educate themselves by their own so it is our responsible to make them educate so that they can save themselves from being iron deficient or getting iron deficiency (Ahmed et al., 2000).

Among all the questioned rural adolescent females, 51.6% had been diagnosed with anemia. The majority (46%) were afflicted with minor anemia, while about one in 20 were in the most severe category. Mild anemia among younger girls aged 10–14 was more common than it was for older girls aged (15–19). Older adults, however, were more likely to have moderate anemia (6.1 percent), but it was less common in the younger group (Kanti Mistry et al., n.d.).

3.2 Iron deficiency in adult women

The incidence of iron deficiency anemia in adult Bangladeshi women has been demonstrated to be influenced by socioeconomic and lifestyle factors (Sultana et al., 2021). Because of the increased iron demand and resultant depletion of iron reserves, iron deficiency anemia is expected to affect more women later in pregnancy. A study of non-pregnant women in rural Bangladesh found a comparable incidence of iron deficiency based on low ferritin levels. When iron deficiency was defined as either plasma ferritin 12g/l or transferrin receptor>4.4 mg/l, the prevalence of anemia was found to be 11% (E. Lindstr¨omet al., 2010). Most women have a higher risk of iron deficiency - they require one and a half times as much iron as men in order to guarantee that they do have enough iron levels. Natural monthly blood loss during menstruation also is clear cause for this. Another less clear cause is that women are more inclined to eat salad than fish, resulting in lower iron intake. During menstruation, a woman removes between 5 and 80 ml of blood, which must be replaced in her bone marrow and spleen. Over a typical menstrual cycle, women lose about 2.5 and 40 mg of iron. This is not a challenge for most women who eat a healthy, nutritious diet, and even a strict vegetarian will have enough iron with some planning. Women with strong or extended menstrual cycles, on the other hand, are at risk of iron deficiency since their iron consumption is always poor, contributing to iron deficiency. To compensate for the higher blood loss of up to 200 ml per menstrual day, they need significantly extra iron. Since more iron is secreted in sweat and urine than normal and higher amounts of energy absorption and oxygen transport takes up more iron also if individuals are really healthy, the iron needs are much higher. Women who are pregnant or breastfeeding, on the other hand, need substantially more iron for the baby they are providing from their own bodies. While pregnant women do not experience the monthly blood loss associated with menstrual cycles, the additional iron required to supply the embryo, shape the placenta, and deliver the additional blood required throughout pregnancy amounts to around 800 mg. As a consequence, pregnant people can eat twice as much iron every day as non-pregnant women. The German Dietary

Association measures and provides daily iron consumption guidelines. Boys and girls have almost the same iron demand before adolescence and the very first menstrual cycle, which rises with age to up to 12 mg a day. Men need just 10 mg of iron per day after their development has been achieved to fulfill their usual iron needs. Due to menstruation, girls and women require more iron than men: 15 mg each day on avg. Women's iron requirements decline to the very same degree as men's after menstruation. These numbers are among those who are in good health. If a doctor suspects iron deficiency, he or she can prescribe a medication to treat the disorder. A well-balanced, nutritious, and well-chosen diet will fulfill men's and women's usual iron requirements. However, as the iron needed is larger, as well as for people who have heavier or more prolonged menstrual cycles, things get more complex. A standard diet is often inadequate in this case, particularly for people who have a moderate, undetected low iron intake. To stay on the safe side, gynecologists sometimes prescribe supplements. Pregnant women, in fact, require more iron to support the fetus; they can take twice as much iron as usual, or 30 mg a day. Breastfeeding women need significantly less iron than pregnant women, with a maximum dose of 20 mg suggested. It's crucial to note that this higher number exists even though someone isn't breastfeeding; she'll need the extra iron in the first few weeks after giving birth to compensate for the blood loss through pregnancy, among many other items (Ahmed, 2000).

Anemia was found to be prevalent in local non-pregnant and non-lactating (NPNL) women in several surveys conducted in 1962/64, with prevalence increasing to 70 percent in 1975, 74 percent in 1981, and 81 percent in 1995. The incidence of anemia was also larger in rural areas than in urban areas, according to the report (Ahmed, 2000). In a national vitamin A survey conducted in Bangladesh in 1997/98, 45 percent of non-pregnant women in rural areas were found to have anemia, while the prevalence of extreme anemia (hemoglobin levels below 70 g l-

1) was less than 1.0 percent. A study of haematocrit values from 2445 non-pregnant people in some districts in 1975/76 indicated a prevalence of anemia of 60%. In 1978, Saha and Ahmad noticed that 70 percent of NPNL women in rural areas with clean water had anemia, relative to 73 percent in areas without safe water. (Hyder et al, 2007) found a prevalence of anemia in a rural community of 159 non-pregnant women aged 20 to 48 years in 1996. In a survey of 63 women employed in Dhaka's textile factories in 1993, 53 percent were anemic (Ahmed, 2000) . Another research comprised 5678 Bangladeshi women of reproductive age, where most of the women (36.7%) were 35–49 years old, and 65.3% lived in rural regions and had iron deficiency anemia. It was found in 41.8% of the population, with 6.8% of women suffering from moderate/severe iron deficieny anaemia and 35.0% from mild iron deficiency anemia (Rahman et al., 2021).

In conclusion, even though the incidence of anemia among non-pregnant women has declined in recent decades, it continues to be a serious health concern.

3.3 Iron deficiency in pregnant women

Iron deficiency has a detrimental effect on mother and fetus health during pregnancy, and has been related to elevated morbidity and infant mortality. Iron deficiency is more common in pregnant women because of the added stress and maternal tissue development it places on the body (E. Lindstr¨omet al 2010) Two separate studies in Bangladesh found that 50 and 59 percent of pregnant women are anemic (Hyder et al., 2004). Breathing problems, dizziness, fatigue, palpitations, and difficulty sleeping are common in affected mothers. They're even more prone to have perinatal diseases, pre-eclampsia, and bleeding. There were also reports of postpartum neurological dysfunction and behavioral issues. Intrauterine growth retardation, prematurity, and low birth weight are all serious perinatal consequences with high mortality rates, particularly in developed countries. Anemia that develops later in pregnancy has a greater effect on fetal development than iron deficiency during the first trimester. This is also applicable in terms of the possibility of early labor. Poor socioeconomic status plays a major role in all facets of these interconnected issues that are more prevalent in developed countries. Both of these contributing and correlating variables can be included in every effective public health or recovery initiative (Abu-Ouf & Jan, 2015).

Iron deficiency anemia can develop after a newborn child's iron reserves are depleted for up to a year. Due to the extreme potential long-term effects, such a condition should be diagnosed and handled as early as possible. Iron is needed for the proper functioning and metabolism of the nervous system. Anemia caused by iron deficiency causes differences in energy balance in the brain, as well as problems with neurotransmitter activity and myelination. As a result, iron deficiency anemia puts babies and young children at risk for behavioral problems including neurological, social-emotional, and adaptive functions. Complications of communication and motor learning have been reported in another research. Breastfeeding is normally protective, but it isn't in the case of iron deficiency in the mother. Iron levels in breast milk have been shown to decrease as lactation continues. For babies who are at risk, careful supervision and proper supplementation are required (Abu-Ouf & Jan, 2015) .

3.4 Consequences of iron deficiency during pregnancy

Pregnancy-related iron deficiency can cause a lot of problems, which is identified as a major public health concern. Pregnant women in low-income countries are said to be impacted 56%, compared to 18% in high-income countries. Preterm pregnancy, low birth weight, perinatal mortality and in the case of extreme anemia, maternal death are both correlated with it (Hyder et al., 2004). Hemoglobin, a protein present in red blood cells that transfers oxygen to tissues, is produced from iron. A pregnant woman needs twice as much iron as a nonpregnant woman during her pregnancy. This iron is needed by the body in order to generate more blood, which is essential for the baby's oxygen supply. They could have iron deficiency anemia if they don't have enough iron stores or doesn't get enough iron when pregnant. Iron needs rise drastically during pregnancy to accommodate an expanding red cell number, a growing fetus, and a growing placenta, as well as any planned or unanticipated blood loss during childbirth, especially with caesarean delivery. According to Scholl, iron needs during pregnancy will reach 1,000 mg, with 500 mg needed for red cell expansion and 300–350 mg needed for the growing fetus and placenta, with differing losses at birth. Surprisingly, pregnant women are seldom screened for ID because they are anemic. Total blood count screening for neonatal ID is indifferent to mild or moderate ID. Permanent ID-related neurodevelopment delay can arise prior to the onset of anemia. In the neonate, more sensitive measurements involve ferritin, zinc protoporphyrin to heme ratios, and reticulocyte hemoglobin material (Juul et al., 2019). The analysis revealed numerous differences in our perception of the harmful impact of maternal anemia and iron deficiency on pregnancy outcomes. Inadequate reporting of anemia's impact on maternal mortality, morbidity, and well-being, as well as child health and growth, are examples of such differences. Maternal IDA raises the risk of preterm delivery and low birth weight, and increasing evidence indicates a correlation between maternal iron condition during pregnancy and infant iron status postpartum. Except in women who begin pregnancy with sufficient iron reserves, iron supplements boost the mother's iron status during pregnancy and the postpartum phase. In the United States, the effects of routine iron supplementation during breastfeeding, regardless of if the mother is anemic, have been hotly discussed, and routine supplementation is not widely performed in all developed countries. Supports regular iron supplementation during pregnancy, while iron supplementation is particularly necessary for pregnant women who experience anemia (Allen, 2000) .

Anemia in IDA in Pregnant and nonpregnant women is described as, in certain clinical practice guidelines; anemia during pregnancy is characterized as Hb 110 g/L or 115 g/L, with minor variations depending on the trimester of pregnancy. A hemoglobin level of less than 100 g/L, on the other hand, suggests anemia at every point of childbirth, which could prompt further study and care due to the possibility of severe effects for the women including intrauterine growth retardation and premature delivery. Meanwhile, anemia in women of reproductive age is characterized as Hb 120 g/L or, in certain reports, 115 g/L, depending on the study and community (Khalafallah & Dennis, 2012) .

While one of the WHO's key goals is to avoid and cure anemia in pregnancy, it is still a poorly understood issue in developed countries, with varying negative consequences based on the nature and extent of anemia as well as the level of pregnancy. Anemia is classified as mild when the hemoglobin level is 10–10.9 mg/dl, normal when the hemoglobin level is 7–7.9 mg/dl and extreme when the hemoglobin level is less than 7 mg/dl, according to the World Health Organization. Several researches have come to conflicting conclusions regarding the connection between mild anemia and adverse maternal and fetal results, concluding that persistent mild anemia will contribute to a typical pregnancy and labor with no negative effects. However, there is mounting evidence that iron deficiency in infants can conflict with deficient myelination, causing long-term deficits in behavioral growth and performance, which may further affect the child's learning ability. Furthermore, treating mild anemia inhibits the development of moderate to extreme types of anemia, which are strongly linked to an elevated risk of fetal–maternal mortality and morbidity, necessitating the use of slightly higher iron doses. Thus, any case of anemia should be managed during pregnancy to avoid unfavorable perinatal effects associated with this condition, with a cut-off of 11 mg/dl being a sufficient cut-off to sustain optimum Hb (10–12 g/dl) during delivery and a stronger overall outcome (Carlo et al., 2015).

Chronic iron insufficiency in placenta can be one kind of consequences caused by iron deficiency during pregnancy. Moreover, physical functions can be impaired as a result of iron deficiency during pregnancy. Additionally, cardiac problem and sudden death also can occur. There is always a risk of maternal morbidity after a postpartum bleeding. There are also some consequences after the postpartum process. Instability of emotion and postpartum depression can also be evident. Finally, milk production can be reduced and there can quick lactation period which can be problematic due to iron deficiency (Carlo et al., 2015) .

3.5 Iron deficiency in overweight women in Bangladesh

Bangladesh is moving through an epidemiologic change, with a rising incidence of overweight and obesity and a high rate of micronutrient deficiencies. The increase in the prevalence of overweight and obesity in the world outweighs the decrease in the prevalence of under nutrition. In countries such As Bangladesh, IDA incidence is mild to high enough to be of public health concern. Bangladesh has seen an unprecedented increase in the incidence of overweight and obesity among women of reproductive age throughout the last two decades. According to research data of Bangladesh Demographic and Health Survey (BDHS) data from 2014, about 34% of urban Bangladeshi women of reproductive age were overweight or obese. Anemia was shown to be prevalent in 37.2 percent of nonpregnant ever-married people residing in metropolitan areas. As per the Bangladesh National Micronutrient Survey 2011, about 7% of reproductive-age nonpregnant and nonlactating (NPNL) people had IDA (International Centre for Diarrheal Disease Research Bangladesh, icddrb, 2013). Several research in this area have looked at the incidence and correlates of overweight and obesity and anemia in women of reproductive age on their own, but none have looked at the coexistence of overweight and obesity with IDA (Ali et al., 2020) .In his research, Ali et al., 2020 found a high prevalence of overweight and obesity between NPNL women of reproductive age with IDA. According to the author's estimates, the prevalence of overweight and obesity among NPNL women with IDA is 43 percent greater than the prevalence of overweight and obesity among all women of reproductive age in rural Bangladesh, which is 34 percent (Ali et al., 2020) .

3.6 Iron deficiency in patients with comorbidity

3.6.1 Iron deficiency in cancer patients

Anemia is a common complication in cancer patients for both diagnosis and treatment, with a multifactorial etiology in the majority of cases. Anemia can occur in about half of patients with solid tumors and hematologic malignancies due to iron deficiency, which is among the most prevalent causes of anemia in this environment. Surprisingly, the attending physician often overlooks this fact, resulting in the failure or postponement of a thorough and timely examination of the iron status. Functional iron deficiency is the most common mechanism in cancer patients, where iron supply is decreased as a result of illness or therapy-related inflammation. As a consequence, serum ferritin does not seem to be a good measure of iron deficiency in this case, while transferrin saturation tends to be more acceptable. The use of erythropoiesis stimulating agents, which improve iron consumption in the bone marrow, may exacerbate the shortage of bioavailable iron. Iron deficiency may induce anemia or exacerbate pre-existing anemia, resulting in a drop in performance and commitment to therapy, with potential clinical consequences. Management of this disorder is still prescribed in several specialist recommendations due to its prevalence and importance, and can be done with intravenous iron if possible. Effectiveness of iron deficiency treatment increases when hemoglobin monotherapy is paired with the erythropoiesis stimulating agents. Slow-release iron formulations have better pharmacological properties and effectiveness in cancer patients than other intravenous iron formulations (Naoum, 2016) .

3.6.2 Iron deficiency in patient with renal failure

The bulk of hemodialysis patients with chronic renal failure (CRF) have anemia. Anemia is caused by an insufficient amount of endogenous erythropoietin in the body (Nissenson& Strobos, 1999). A shortage of iron in chronic kidney disorder is associated with anemia. Absolute and functional iron deficiency is common in patients with CKD. Functional iron deficiency is characterized by appropriate iron stores but inadequate iron supply for integration into erythroid precursors, while absolute iron deficiency is described by significantly diminished or missing iron stores. Hepcidin levels have risen, which is the cause of this. Anemia is linked to a higher incidence of morbidity and mortality in patients with chronic kidney disease (CKD). The seriousness of anemia can play a role in the relationship between anemia and mortality. Also, at primary CKD diagnosis, all CKD patients should be checked for anemia. As CKD is related to natural renal activity, the criteria used to describe iron deficiency may vary. Whenever the transferrin saturation (TSAT) is less than 20% and the serum ferritin concentration is less than 100ng/mL in pre-dialysis and peritoneal dialysis patients, or 200ng/mL in hemodialysis patients, total iron deficiency is diagnosed. TSAT of less than 20% and elevated ferritin levels are signs of functional iron deficiency, also known as iron-restricted erythropoiesis. Both CKD patients who suffer from anemia should take iron supplements. According to recommendations, intravenous iron supplementation is the optimal option for CKD patients on dialysis (CKD stage 5D), and either intravenous or oral iron supplementation is prescribed for CKD ND (CKD stages 3–5) patients (Gafter-Gvili et al., 2019).

3.6.3 Iron deficiency in patient with heart failure

Iron deficiency in individuals with cardiac insufficiency is a highly widespread co-morbidity involving up to 50% of all outpatients. It's also correlated with decreased ability to exercise and lower levels of physical well-being (von Haehling et al., 2019).

Iron deficiency anemia is common amongst patients with cardiovascular insufficiency with an estimated prevalence of more than 50 percent. It is a separate predictor that functions and survival are worse. Defining the deficiency of iron in cardiac insufficiency differs from other chronic inflammatory conditions and is: ferritin < 100 μg/L, or 100-299 μg/L ferritin with saturation of transferin <20 percent. Intravenous iron (IV) is currently the favorite treatment route in patients with heart insufficiency. In the majority of studies, IV iron sucrose or ferric carboxymaltose (maximum 200 mg per setting). To date, in patients with heart failure with reduced ejection, no clinical trial has demonstrated the efficacy of Oral iron. In addition, oral iron preparations are linked to a high rate of adverse effects (in up to 40% of the patients), poorly absorbed by intestinal wall oedema, and iron stores can be replenished for up to six months. The guidance of the European Society for Cardiology of Cardiomyopathy recommends the testing of serum ferritin and transferrin saturations by all patients with heart failure. In patients with symptomatic heart failure with iron deficiency, the European Guidelines recommend treating IV ferric carboxymaltoses to improve symptoms of heart failure and quality of life. There is no specific formulation recommended by the US guidelines, but IV iron is recommended as a Class IIb, Evidence B Recommendation in patients with heart defect and iron deficiency. The role of iron was not established in patients with heart failure and preserved expulsion. A clinical trial is in progress and this is being assessed (von Haehling et al., 2019) .

3.7 People who have undergone major surgery or physical trauma

According to one comprehensive study, anemia is normal in the pre-operative environment, with rates varying from 11 percent to 76 percent. Many research on the assessment and treatment of perioperative anemia focus on patients having significant orthopedic surgery, with one finding that 35% of patients have hemoglobin levels less than 13 g dl at preadmission examination. Of note, the incidence depends based on the surgical community, with a prevalence of up to 75% of people having colon cancer surgery (M. Muñoz et al., 2017)

3.8 Iron status of women in associated with iron concentration in ground water in rural Bangladesh

The risks are high for women of reproductive age, often due to diets with a low content of bioavailable iron. In certain circumstances, the iron content of domestic groundwater sources was high but the intake and status of iron was not considered. Researchers assessed the connection between groundwater iron intake and iron status in a rural Bangladeshi percentage of women with dietary iron deficiency. The iron deficiency definitely attributable to iron consumed by the drinking groundwater was not reproductive, and was a major contributor to dietary intake. Researchers found a favorable correlation between plasma ferritin and total body iron and daily iron consumption from groundwater in northern Bangladesh, which was 0.42 mg for half of the female population. There was only a very slight increase in iron overload, but a strong dose-response relationship exists between natural iron content in groundwater, intake of iron from these sources, and women's iron status, such that body stores should be 0.3 mg/kg higher for every 10-mg increase in daily iron intake from water. This suggests that local water intake had a significant and beneficial impact on rural residents' iron status, nearly eradicating iron insufficiency while presenting no dangers related to excess iron, according to the study's estimates of their plasma ferritin levels. The findings of the author suggest that iron intake from water in such settings should be included in diet tests. A study found that iron consumed by drinking groundwater is positive for iron conditions and is likely to be a main contributor to preventing iron deficiency when bioavailable iron diets are otherwise low. When evaluating dietary risks associated with iron deficiency, iron intake should be taken into account through water (Merrill et al., 2011)

Chapter 4: Diagnosis

4.1 Different diagnostic tests.

Iron deficiency can be diagnosed by different tests as described below

Red blood cell size and color

Red blood cells appear thinner and more colorful than average in iron deficiency anemia.

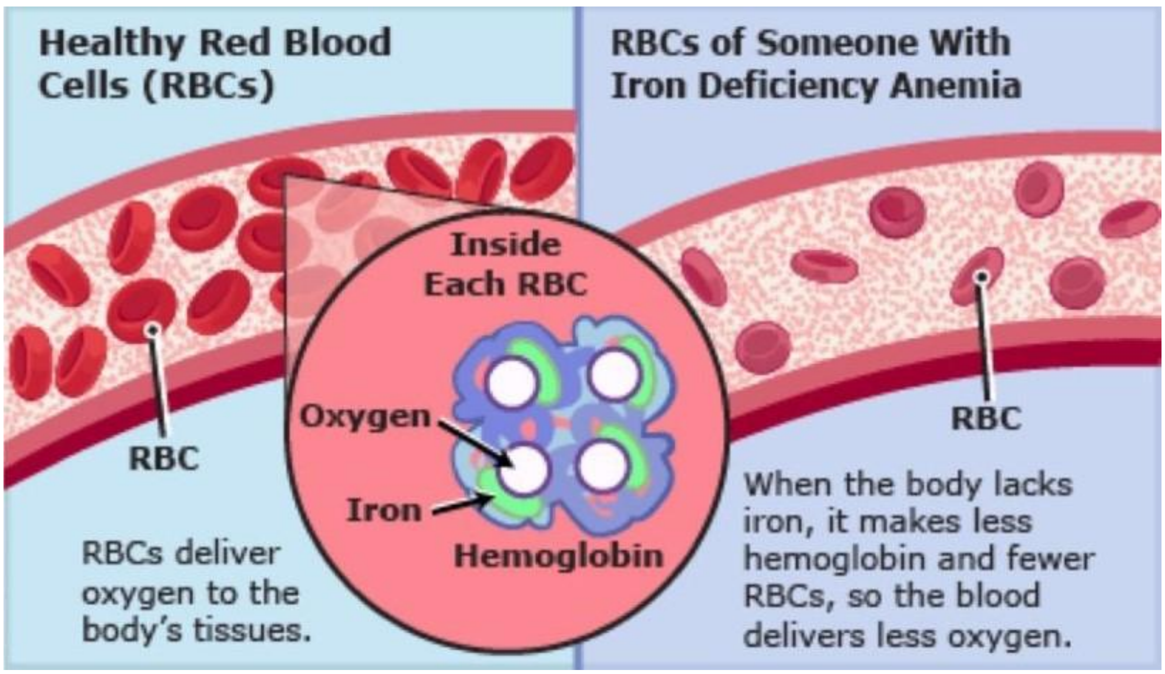

Figure 1: Red blood cells during iron deficiency (Adapted from: tracy et al., 2018)

Hematocrit level

This is the proportion of red blood cells that make up the patient's blood volume. Standard ranges vary from 35.5 to 44.9% for adult females and from 38.3 to 48.6% for adult males. Based on age, these values can shift. Iron deficiency is seen in decreased level of hematocrit

(Hemoglobin:- Part 4 – Hematocrit (HCT, Hct), Packed Cell Volume (PCV) – Labpedia.Net, 2007).

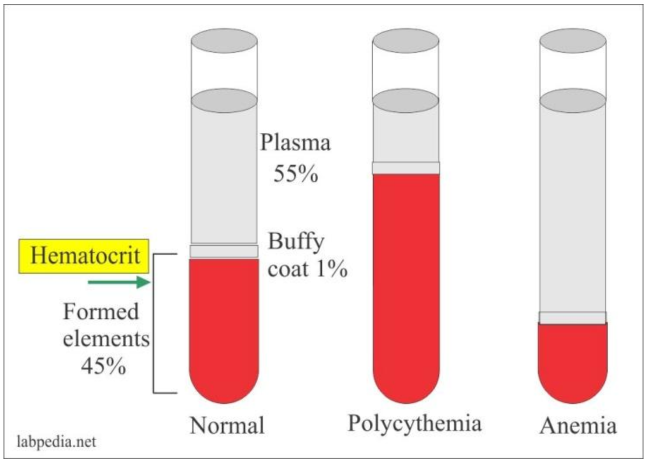

Figure 2: Hematocrit values in iron deficiency anemia (adapted from: labpedia.net, 2007)

Hemoglobin level

Iron deficiency Anemia indicates lower than average amounts of hemoglobin. The natural level of hemoglobin for males is commonly described as 13.2- 16.6 g/dL for women and 11.6-15 g/dL for men.

Screening of Serum Ferritin level

This protein helps in storing iron in the body and low ferritin levels generally mean a low stored iron level.

The screening measure for iron deficiency is serum ferritin. The children's ferritin cut-offs vary from the adult ferritin cut-offs.

- The diagnosis of iron deficiency is <12 ug/L ferritin.
- The iron defects are probable with Ferritin 12-20 ug/L. One should take iron supplementation into consideration.
- In pre-pubertal infants, Ferritin >20 ug/L shows usual iron stocks. The prescribed cutout of ferritin for children is smaller than for adults, since children may not have enough time to build iron stores and since the tissue develops demands iron (Manuel Muñoz et al., 2010)

4.2 Additional diagnostic tests

When iron deficiency anemia is present in the patient's blood, the doctor can order more tests to detect an underlying cause (Z. Fireman et al., 2006).

Endoscopy

Physicians also examine endoscopy for leakage of the hiatal hernia, ulcer, or stomach. During this process, one's throat is moved to his/her stomach by a short, lighted tube fitted with a video camera. This encourages the specialist to check for sources of leakage from the mouth to liver (esophagus) to the belly. Endoscopists are often tasked with determining the cause of bleeding and evaluating iron deficiency anemia. GI studies in premenopausal women with IDA have shown little results in this study. Because of the iron loss related to menstruation and pregnancy, women are more likely to have an iron deficiency throughout their reproductive years. Several studies have shown that among premenopausal women with iron deficiency anemia, gastrointestinal sources of chronic blood loss affect 28 of the 43 women. These findings indicate that bi-directional endoscopic examination of the gastrointestinal tract will help this group (Z. Fireman et al., 2006).

Colonoscopy

Physicians can prescribe a process called colonoscopy to rule out lower intestinal causes of bleeding. The rectum is fitted with a small, versatile tube with a video camera and directed into the colon. Throughout this exam, patients are normally sedated. A colonoscopy test helps the physician to look for potential leakage inside or inside the colon and rectum. Low iron levels in patients with iron deficiency anemia may be a sign that they should undergo a colonoscopy. If anyone has iron deficiency anemia, it may be a symptom of colon polyps or possibly colon cancer. Bleeding from the esophagus, stomach, or duodenum may lead to iron deficiency anemia as well as other health problems. Often, the doctor may suggest an upper endoscopy along with a colonoscopy in such situations. To find out whether there is internal bleeding or colon cancer, the doctor may suggest having a colonoscopy as well as an upper endoscopy if there is an indication of iron deficiency anemia (M.R. Stephens et al., 2006).

Ultrasound

Women may still seek the source of excessive menstrual bleeding, for example, uterinal fibroids through pelvic ultrasounds.

Chapter 5: Treatment options available to cure iron deficiency anemia

5.1 Supplementation of iron, vitamin A and zinc

Research has been undertaken to identify ways to enhance normal iron care and correction of iron deficiency anemia for women in Dinazpur, Bangladesh, by the inclusion of extra vitamin A alone or in conjunction with zinc (Kolsteren et al., 1999) .

The 3 care classes were allocated to randomly 216 non-pregnant women of 15-45 years old with hemoglobin levels ≤100 g/l. The iron (A) group, the iron and the vitamin A second (B) groups and the iron, vitamin A and zinc third (C) groups were obtained. Every female was provided 60 days of a FeSO4 comprising 60 mg of elemental iron for one iron capsule per day. Furthermore, on the first day of therapy following processing of blood sample, groups B and C obtained 200 000 IU of vitamin A, taken as a supervised dosage. Group C got zinc gluconate of 15 mg elementary zinc every day for 60 days (Kolsteren et al., 1999) .

Of the 328 women surveyed, the hemoglobin amount was 254 (77.5%) ≤100 g/l and 322 (98%) ≤120 g/l. With the exception of serum iron in the iron group, the three therapy schedules greatly raise hemoglobin levels and boost iron parameters. Compared to the iron-alone community (13.4 g/l), the group that got iron, vitamin A and zinc was better at resulting to a 17.9 g/l rise in hemoglobin. The intermediate reaction of iron and vitamin A therapy was 15.9 g per liter. But only in the community consuming iron, vitamin A and zinc and only for the rise in hemoglobin are these variations statistical relevant, P=0.03 (Kolsteren et al., 1999)

The findings indicate that adding vitamin A and zinc to the iron deficiency treatment can raise the quantity of hemoglobin more than with iron alone. Pretty much across the board, a single dose of vitamin A applied to iron therapy could not be established by current research. Adding zinc to the medication scheme yielded improved outcomes, but the overall limited reaction to therapy should be read quite carefully. This limited answer underlines the significance of other deficiencies as possible, in developing countries with high levels of malnutrition, of hampering the response to iron-deficiency anemia (Kolsteren et al., 1999) .

5.2 Dietary intake

Including iron-rich meals into the regular diet is the most powerful option to prevent IDA. The prescribed regular allowance now referred to as dietary intake, lists quotes for daily usage in all populations: males need 10 mg daily; females need 15 mg daily and females who are going with pregnancy need at least 30 mg daily (Kolsteren et al., 1999) .

But there can be limits to proper intake: foods of this type may be too high, scarce or not preferable; iron's bioavailability from fruit and vegetables (non-heme food) may be considerably lower (1 percent to 10 percent) than the bioavailability from meat (heme food) at only 20 to 30 percent. The phytaticphytats in legumes, pasta, and seeds inhibit uptaking iron (Brody, 1999; FAO/WHO, 2004; Zohouri& Rugg-Gunn, 2002) by 50 percent. By comparison, vitamin C foods can improve the uptake of nonheme foods by 200% to 300% (FAO/WHO, 2004). Furthermore, fruit and vegetables generate excessive organic acids that help absorption, whereas vitamin A precursors of B-Carotene in the presence of phytats or tannic acid are capable of overcoming its inhibitory impact. However, no improvement effects of vitamin A on nonheme iron absorption have been identified in one review. Cooking in iron pots on a regular diet will also raise the amount of iron. Methods to support consumers optimize and adjust their diets to promote sufficient intakes and absorption of iron must be specifically established (Kolsteren et al., 1999).

Table 2: Bioavailability: Enhancers and Inhibitors of Iron Uptake

Enhancers	Inhibitors
1. Vitamin A	1. Calcium, especially from milk and milk products
2. Vitamin c	2. Drinking tea, coffee, or cocoa with meals
3. Fresh fruits and juices	3. Certain spices like oregano
4. Vegetables	4. Antacid
5. Fermented foods (sauerkraut and soy sauce)	

Source: Adapted from the Food and Agriculture Organization/ World Health Organization (2004) and the World Health Organization (2001).

5.3 Blood transfusion

Rest and nutritional alterations are also adequate for iron deficiency resolution. Often, though, blood transfusions might be required to save life, this may be part of the regular therapy to aid with iron deficiency management.

A blood transfusion is a regular medical operation where a specialist passes the blood from a donor through the veins to the person in need. People will obtain it via this process:

- Blood entirely

- Red blood cells
- plasma
- platelets

Even though people donate whole blood sometimes, which contains many of the above blood components and white blood cells, physicians also do not include them in transfusions. Preoperative anemia is a strong indicator that a patient may need blood transfusions after surgery. Peri-operative blood loss is the most common cause of postoperative anemia in surgical patients, and inflammation-induced suppression of erythropoietin and functional iron shortage may increase the condition. The typical human has around 5 liters in the body and part of the missing blood is replaced by blood transfusion. Through injecting a plastic tube into the vein, the blood is provided intravenously through the patient's vein. The transfusion of blood substitutes the red blood cells with fresh iron-bearing cells primed for oxygen to be conveyed throughout the body. But certain individuals do not want a blood transfusion and are free to reject it. This rejection could arise from personal convictions or other causes and an appropriate cure could be a transfusion of iron (M. Muñoz et al., 2008).

5.4 Parenteral iron therapy option

Parenteral iron therapy is also required for oral iron therapy, for recommended erythropoietin therapy or for use in the treatment of functional iron failure. Three drugs are now available: iron dextran, ferric gluconate and iron sucrose (Silverstein & Rodgers, 2004)

Hepcidin, a peptide hormone produced mainly by the liver, monitors iron absorption and regulation (Percy et al., 2017) . The effective treatment of ID and Iron Deficiency Anemia (IDA) using oral formulations, parenteral iron or blood transfusion is critical to understanding the metabolism of iron. The iron content in oral formulations varies with gastrointestinal symptoms. In cases of compliance/tolerance problems with oral iron, comorbidities that may impact absorption or continuous iron losses that surpass the absorption capacity, parenteral iron should be indicated. It may also be the best choice if rapid iron reproduction is essential to avoid physiological degradation or preoperative for non-delayed surgery. We will now lead the way in terms of ID/IDA diagnosis, management, and treatment initiation. This management improves their quality of life dramatically.

Iron dextran has existed in the US for over 40 years, and its potency and toxicity have considerable medical knowledge. Since iron dextran-induced anaphylaxis is related to death and less serious allergic reactions, several physicians oppose the use of this medication. In recent years, two additional parenteral iron drugs have been cleared for use in the United States by the Food and Drug Administration (FDA). In dialysis patients, a comparative analysis has been performed on the efficacy of parenteral iron preparations (Silverstein & Rodgers, 2004) .

The two newer drugs (ferric gluconate and iron sucrose) were used in Europe for more than 30 years, but recently their legalization has been in the USA. The particular approval from the FDA for the new medicines is for iron deficiency anemia in chronic renal disease and in erythropoietin supplementation for hemodialysis patients. However, these drugs are also used off-label to treat some sources of iron deficiency, and 'functional iron deficiency' has been identified in cancer and renal failure patients on dialysis (Silverstein & Rodgers, 2004)

5.5 Routes of Iron therapy

The iron therapy intravenously has been commonly used for patients with saccharated iron oxide since (Nissim,1947) treated anemic patients, which has been very effective in patients with refractory iron caused by malabsorption or other causes such as rheumatoid arthritis. Intravenous iron is normally a good response for patients who are intolerant of oral iron. The downside of this type of treatment is that the iron administered intravascular precipitations cause reactions both early, because of an allergic condition and later (Nissim, 1954). The above is also lethal, so it is advisable to prepare parenteral iron instead and less dangerously (Baird & Infirmary, 1953)

5.5.1 Intramuscular iron therapy

Different trials also provided intra-muscular details on the benefits and necessities of iron therapy. Parenterally delivered iron was consumed and used intramuscularly. After just one 4 or 5 ml intramuscular infusion, serum-iron levels in both anemic and stable individuals achieved a variable high within one or two days and returned to approximately usual after six or seven days. After the preparation was injected, there were no signs of elevated urinary excretion of iron. The iron injected is gone from the serum slower than the iron oxide. No harmful reactions have been detected following intramuscular injections, despite serum-iron amounts of 13-8 mg per 100 ml (Baird & Infirmary, 1953)

Of the 40 incidents, 38 of intramuscular therapy with iron preparation are appropriately referred to. 43 mg of iron will increase Hb intramuscularly by 1%, with the greatest increase occurring after 4-9 weeks (Baird & Infirmary, 1953).

5.5.2 Intravenous iron therapy

Intravenous iron therapy is becoming increasingly popular. It is common since modern formulations are efficient, usually tolerated well without any worry about the rate of absorption or the side effects of oral treatments. This led to a paradigm shift in iron therapy, with the latest high dose preparations being prescribed steadily increasing. While intravenous iron infusions are possible in the overwhelming majority of patients, the possibility of serious infusion reactions remains low. In the majority of patients with retained renal function, particularly ferric carboxymaltose causes hypophosphatemia. Thorough study of iron preparations indications and pharmacodynamics can inform clinicians when selecting the best medication for a patient at the appropriate moment in their course of disease (Schaefer et al., 2020)

Nanoparticles made from ferric oxy-hydroxides and carbohydrates are modern formulations of intravenous iron (Jahn et al., 2011; Neiseret al., 2015). The addition of saccharized iron oxide, which can have adequate tolerance of up to 500 mg in doses (Nissim and Robson, 1949), was a significant advancement in the development of a stable intravenous iron preparation (Schaefer et al., 2020)Iron dextran (ID) was found to be very well tolerated when intravenously injected in pursuit of other iron preparation (Treatment et al., 1964). The new iron preparations, including ferric carboxymaltose (FCM) (Vifor (International), 2018, 2020, ferric derisomaltose (FDI, formerly known as iron isomaltoside 1000), and ferrumoxytol (FMX), were created to increase tolerability of iron formulations thus enabling large iron doses substitution.

5.6 Different molecular weight iron dextran

Parenteral iron is offered in a number of formulations for patients, including molecular iron dextran products called high-(HMW) or low-(LMW) molecular iron dextran. While the chance of unhealthy accidents is increased, HMW iron dextran may be replaced by LMW iron dextran with little knowledge of the doctor due to cost reasons. The Centers for Medicare and Medicaid Services (CMS) has recently taken the decision to reintegrate J-codes for all iron dextrans, which could improve the accidental usage of HMW Iron Dextran. Doctors that use parenteral iron should be mindful of these practices and engage regularly in formal replacement decisions (Neilson, 2008)

In the mid-1990s, the prescriptions of nephrologists were affected by two cases. Initially, high molecule iron dextran was withdrawn from the market and eventually low molecule iron dextran was released. The normal treatment method for patients with hemodialysis anemia was low molecular-weight iron dextran. A further high-molecular iron dextran product (DexFerrum [American Regent]) was published shortly afterward for therapeutic use (Auerbach & Rodgers, 2007)Although iron dextran has been in use for almost 30 years and has been well known for efficacy, a better safety profile was obtained by introducing low molecular iron dextran in 1992 (Ayub et al., 2008) .

Body iron reserves are rehabilitated more quickly by intravenous iron and a quick rise of hemoglobin will be more probable. The only disadvantage of intravenous therapy is the requirement for brief or at least ambulatory hospitalization for tight observation (Ayub et al., 2008) . And low molecular weight iron dextran is more effective in this route, which has been proven already.

5.7 Different types of iron preparations

The iron shortage will not be resolved overnight, and this is necessary to take iron supplements for several months or longer to replenish the iron stores. In general, after around a week of therapy an individual can begin to feel stronger. Different iron preparations can help to increase the iron storage in body by which one can solve the problem of iron deficiency. An oral iron preparation called Monoferric® (ferric derisomaltose) was approved by the FDA for the treatment of iron deficiency anemia (IDA) in adults who have a physical aversion to iron or who did not respond well to oral iron. The approval was also provided to adult patients with non-hemodialysis based chronic kidney disease who have an intolerance to iron or who have an unsatisfactory reaction to iron (*FDA Approves Single-Dose Injection Therapy for Iron Deficiency in Adults*,2016). Different types iron preparations are described in below.

5.7.1 Ferrous sulphate

The ferrous sulfate iron substitute is an iron salt with the FeSO4 chemical formulation. One form of mineral iron is Iron Salt. They are also used to treat iron deficiency as a replacement. The biggest advantage is the maintenance of natural iron levels in the body by taking ferrous sulfate supplements. This will protect anyone from developing iron deficiency and from experiencing a variety of moderate to extreme side effects frequently associated with it (Leary et al., 2015).

A research aimed to characterize serum iron pharmacokinetics in non-pregnant women with iron deficiency Anemia (IDA) after single oral administration of a lengthy released ferrous sulphate tablet. In 30 women aged between 18 and 45 with IDA, a multicenter, single dose, open-label research was performed. In fasting settings, 2 tablets of 80 mg ferrous sulphate have been taken as a single 160 mg oral dose of ferrous sulfate. This research shows the optimum long-term release of iron in the gastrointestinal tract in the selected population through an oral dose of 160 mg ferrous sulphate given under a rapid condition to 30 women with IDA. This enables elevated serum iron levels to be achieved and maintained up to 12 hours after administration (Leary et al., 2015)

Mechanism of action of ferrous sulphate:

In the red blood cells, myoglobin, and other heme enzymes in the body, ferrous sulfate replaces iron reserves found within hemoglobin. Ferrous sulfate also enables oxygen to be transported by hemoglobin. Roughly 60% of iron is held in red blood cells in hemoglobin, while 9% is contained in myoglobin and other hemic enzymes. In addition, 25% of reticulocytes of the liver, spleen and bones are kept in reserve.

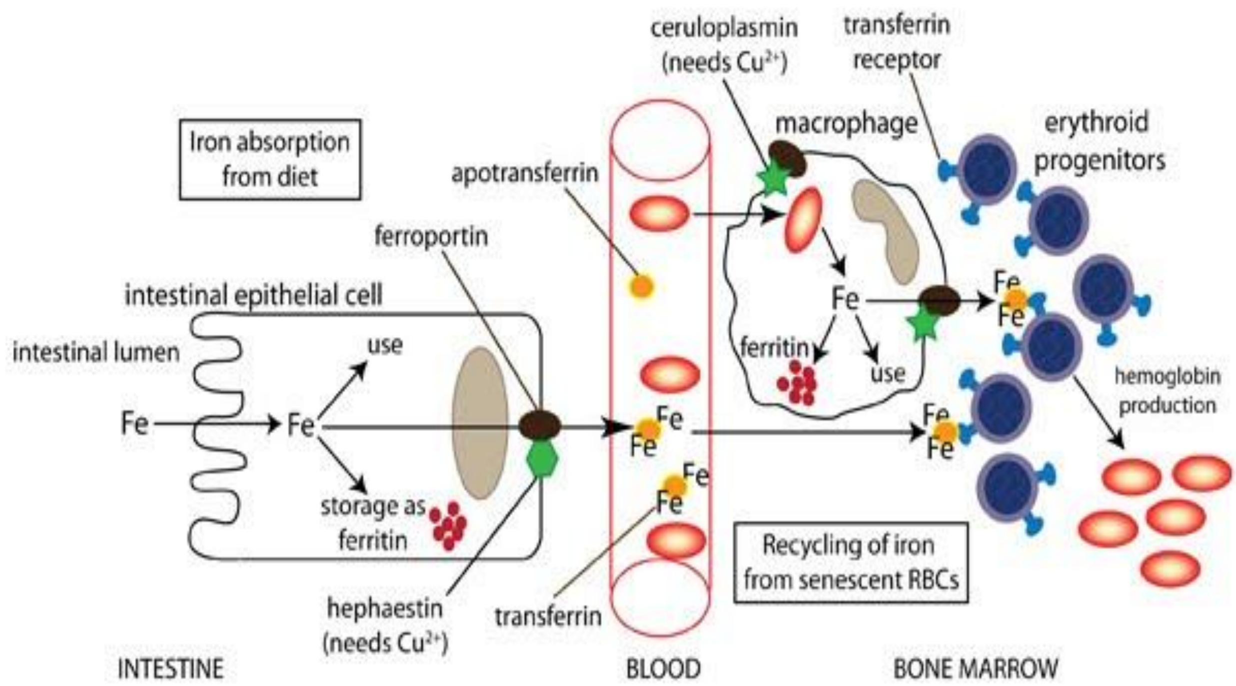

Figure 3: Mechanism of action of ferrous sulphate (adapted from: parvin et al., 2012)

Any of the iron contained is linked to ferritin protein (figure-3). Fe2+ iron is transformed into Fe3+ by ceruloplasmin while it is transported to the body so that it can be attached to protein transferrin.

5.7.2 Ferrous gluconate

If anyone has problems taking iron supplements with nausea, ferrous gluconate is also even better tolerated. Ferrous gluconate contains very little iron than ferrous sulfate per dosage. A disadvantage of ferrous gluconate is that it is not absorbed as readily as sulfate. This is because of the inorganic molecule of gluconate. For the liver, it's difficult to separate two inorganic substances, which means one absorbs less. For the liver, it's difficult to separate two inorganic substances, which means one absorbs less. Researchers said, ferrous gluconate remains an excellent choice – approximately 90% of the ferrous sulfate absorption rate (Jaber et al., 2010).

Research reveals that supplements of iron polymaltose (IPC) and iron gluconate (IG) are efficient in preventing iron deficiency. The lower number of children living with hemoglobin < 11 g/dL and slightly more average hemoglobin of IG groups showed, nevertheless, that IG was more successful than IPC. Around the same period, IG was correlated with a higher average impact incidence and a higher rate of attrition. Given the subsequent concurrent results of the same group, the authors speculate that although the reasons for dropping out of the sample were not always known, they were presumably due in certain instances to the harmful effects of the drug. In this context, ferrous gluconate and IPC are both appropriate drugs. Iron gluconate is powerful, but less tolerable than IPC. When deciding on prevention or therapy, physicians may take this into consideration (Jaber et al., 2010).

Pharmacodynamics

Hematinic action: Ferrous gluconate substitutes for iron, an integral part of hemoglobin production.

Pharmacokinetics

Absorption: The duodenum and proximal jejunum are absorbed in the GI tract, however their main absorption sites. Up to 10% of iron is ingested into the healthy patients; iron-deficiency anemia patients can consume up to 60% of iron. The consumption of food may be reduced from 33% to 50% (*ferrous gluconate*, 2017.) .

Distribution: Iron gluconate is transferred directly into the blood by GI mucosal cells, automatically attached to a carrier protein, transferring, and carried into a bone marrow for hemoglobin incorporation. Iron is very protein-like.

Metabolism: It is released through hemoglobin degradation but preserved and reused across the body.

Excretion: Healthy people sacrifice no iron every day. Men and women lose approximately 1 mg/day, while women in premenopausal lose approximately 1.5 mg/day (*ferrous gluconate*, 2017.)

5.7.3 Iron polymaltose complex

The Iron (III)-polymaltose hydroxide complex (IPC) is a solid iron and polymaltosis iron preparation. IPC has lately become a subject of much discussion about its utility in the treatment of iron deficiency anemia (IDA). Adverse reactions were less often notified to IPC (14.9%), especially in the case of high digestive disorder, stains, and diarrhea, than with ferrous sulfate (34.1%; $p < 0.001$) (Toblli & Brignoli, 2007) .

The meta-analysis of the trials of adult iron deficiency anemia in comparable doses of IPC with iron sulfate shows that the two compounds also achieved equal amounts of hemoglobin to indicate a similar degree of efficacy. The tolerance of IPC in adults clearly improved compared to ferrous sulfate; for individual adverse reactions, too, the differences were large. This is potentially due to an improved risk/benefit profile of IPC in adults. Randomized controlled trials are required, particularly in pediatrics (Toblli & Brignoli, 2007) .

In the intestine, iron from IPC is consumed by a self-limiting competitive exchange of ligands, causing the intestinal delivery pathway to become saturated in the event of an overdose. As a result, IPC intoxication by accident is uncommon. The LD50 of ferrous sulfate is 350 mg/kg, according to (Geisser, 2011), while the LD50 of IPC cannot be determined even at doses exceeding 2000 mg/kg (Toblli & Brignoli, 2007)

The Iron Polymerase Complex (IPC) seems to be starting to be a little more sluggish than conventional iron salts. A significant distinction between IPC and ferrous salt is that when IPC is taken with meals, bioavailability is also improved, which is the preferred treatment process.

IPC is recommended as an oral iron therapy for iron deficiency treatments, such as iron deficiency Anemia, iron deficiency care (iron store depletion) and for iron deficiency prevention during breastfeeding and lactation. IPC is designed to be used for iron therapies. IPC has been active, in addition, in the reproduction and correction of iron deficiency in babies and small children with iron stored in daily blood donors with and without Anemia. IPC is well accepted in general and tends to induce substantially less stomach disturbances than ferrous salts. In certain clinical studies, the frequency and gravity of adverse effects was smaller for IPC compared to iron sulphate. In unintended overdose situations, IPC is often better, although there were no reports of deaths. Recent research has shown that ferrous sulfate could be related to oxidative stress response, but it does not refer to IPC. Considering the therapeutical comparable concept, if two preparations show the same effectiveness and protection, the IPC is preferable as iron salts because it has the same potency, but has a better safety profile (Geisser, 2011) .

5.7.4 Iron sorbitol

Iron Sorbitol is a complex of dextrin and sorbitol in stabilized form with ferric, sorbitol and cytric acid. It can be used after oral therapy is unsuccessful or unsuitable in the management of proven iron deficiency Anemia. Parenterally, iron Sorbitol is given. Following parenteral administration, severe anaphylactoid responses can occur. It is often classified as Iron Sorbitex. It comes from synthetic origin and belongs to iron salts. Iron Sorbitol is 415.39 in molecular weight. The benefits of iron sorbitol in comparison to iron sucrose are low therapeutic costs (Wali et al., 2002) .

5.7.5 Iron isomaltoside

Iron Isomaltoside is used to treat iron deficiency or iron deficiency anemia. It fills up the body's iron reserves. Iron Isomaltoside is used for regulating human body hemoglobin levels. Patients with iron deficiency are normally administered. The doctor may recommend patients to use this drug before the amount of hemoglobin is normal (Frigstad et al., 2017) .

Under the guidance of a qualified health care provider or a specialist, only iron Isomaltoside should be prescribed and should not be automatically administered. The dosage depends on the situation under which patients are treated and the doctor decides on that. Because of the isomaltoside, one may gain weight. Iron Isomaltoside is susceptible to constipation or acne (Frigstad et al., 2017).

Iron isomaltoside enables effective and well tolerated iron deficiency therapy, and additionally, the requirement for retreatment is reduced over time by elevated doses. Several patients became anaemic following surgery, which indicated that regular doses of complete iron adjustment were ineffective. Infusion reactions, close to those recorded in clinical trials, were reported in 2% of patients (Frigstad et al., 2017) .

5.7.6 Iron sucrose

Iron sucrose injection is an iron replacement agent that is used to manage anemia and iron deficiency in chronic renal disease patients. The iron sucrose, which was available clinically about 70 years ago in 1949, is one of the first IV iron preparations to be made. This treatment is the most widely practiced in the world, with 25 million patients' years of clinical experience. Many trials in a wide variety of therapies consistently show, in addition to encouraging erythropoiesis, that iron sucrose can correct iron deficiency and thereby reduce the necessary dosage of erythropoiesis stimulating agents (ESAs). It is not only competitive with iron sucrose; it is well tolerated and improves biodisposable iron supplies rapidly (Macdougall et al., 2020) .

In a broad range of conditions, that trigger and are linked to iron deficiency and iron deficiency anemia, the efficiency of iron sucrose. The treatment for iron sucrose under these different circumstances is correlated with enhanced iron status (ferritine, TSAT); increased Hb levels, with or without ESA therapy; improved quality of life relative to health and clinical results. In combination with ESA treatment, iron sucrose significantly decreases the criteria for ESA doses (Macdougall et al., 2020) .

In comparison with oral therapy, the application of iron by IV iron sucrose is effective for several benefits. Iron sucrose has shown itself capable of raising Hb levels with or without ESA treatment, as well as improving ferritin and TSAT levels. The IV administration of iron sucrose overcomes poor absorption of the intestines and decreased release of iron that can delay oral therapy. Overall, hematologic responses with iron sucrose are obtained more quickly and reliably than through oral iron administration, which will help ensure the usage of iron sucrose is cost efficient when considering decreases in ESA doses and reductions in supplementary medications for the treatment of anemia in patients. Unlike previous days, when iron sucrose is administered, the EMA doesn't need a test dose. It is also well absorbed and improves bioavailable iron reserves quickly as well as iron sucrose. This is critical for people who cannot withstand oral iron therapy, who fail to comply with oral care, or who do not have oral preparations. Treatments of iron sucrose with an appropriate safety profile are especially advantageous because of its potential to raise saturation levels of hemoglobin, ferritin and transfers quickly (Macdougall et al., 2020) .

5.7.7 Ferric carboxymaltose

The iron substitute substance is ferric carboxymaltose. In adulthood, the treatment for anemia of iron deficiency is ferric carboxymaltose. Ferric carboxymaltose is normally administered if it has not been taken orally (by mouth). Ferric carboxymaltose is a hydroxide colloidal iron (III), complex with carboxymaltose, a carbohydrate polymer which releases iron needed for hemoglobin, myoglobin and specific enzyme systems (*Ferric Carboxymaltose (Professional Patient Advice) - Drugs.com*, n.d.) . Ferric carboxymaltose is a non-dextran formula that permits iron uptake without releases of free iron (Szczech, 2010).

The effectiveness and protection of Ferric carboxymaltose (FCM) during pregnancy were studied in different case control research. In the baseline case group, FCM therapy improved Hb effectively to amounts that had been present in the control group. In the case groups and groups receiving postpartum FCM, no hypersensitivity, any anaphylactic reactions or any other harmful effects were identified. The results between the case and the control group were both fetal and maternal (Pels & Ganzevoort, 2015) .

5.8 Erythropoietin

The supplementation of iron is not often enough to cure pregnant anemia quickly and effectively. Despite its problematic application and protection, blood transfusion is commonly used to treat serious or resistant pregnancy anemia. Many women reject transfusion of blood due to the possibility of complications including bacterial diseases or non-infectious and immunological consequences. As an option for blood transfusion and as a medicinal means to anemia with chronic renal failure with low endogenous erythropoietin production, synthetic agents such as recombinant human erythropoietin (rHuEPO) have been developed. Over the past 10 years, supplements of rHuEPO have also been used in maternity and postpartum iron deficiency anemia treatment. However, certain fertility treatments remain problematic and limited-use while more explanation is needed on several questions relating to indications, dose and protection (Sifakis et al., 2001)

5.9 Consultation and long-term monitoring

Proper consultation is required for the patients who are affected with iron deficiency. They should be consulted with proper medicines and guidelines should be given by the physicians and the pharmacists. Proper dietary plan should be given to fight against iron deficiency by improving the immunity of the patient.

Outpatient iron deficiency monitoring ensures that iron treatment is adequately responded to and that iron therapy is continued to replenish body iron reserves until Anemia is corrected. Follow-ups might also be necessary in the treatment of any iron deficiency underlying cause.

5.10 Natural dietary sources

Different natural dietary sources to fight iron deficiency are given below:

Table 3: Natural dietary iron sources

Iron from animal foods	Iron from plant foods	Other iron sources
1. Old beef meat.	1. Spinach	1. Seaweeds
2. Beef liver/Chicken liver	2. Lentils, Chickpeas	2. Herbal teas
3. Eggs	3. Kidney beans	3. Blackstrap molasses
4. Oysters and turkey	4. Quinoa	
5. Lamb	5. Pumpkin seeds	

Chapter 6: Treatment induced adverse effects

6.1 Adverse effects of increasing dietary iron intake

Around 3.3 million women of childbearing age and 240,000 infants between 1 and 2 years of age have anemia of iron deficiency. Hemochromatosis is a hereditary disorder which is marked by excessive accumulation of iron, storage of excessive tissue and possible damage to tissue. Typically, between 40 and 60 years of age, if iron overload is undetected and untreated, morbidity (e.g., cirrhosis, hepatomas, diabetes, cardiomyopathy, arthritis or athropathy) might occur. Clinical excess expression of iron relies on the seriousness of metabolism, the availability in the diet of an adequate amount of absorbable iron and physiological depletion of blood from the body (e.g., menstruation). The suggested hemochromatosis test for transferrin saturation; hemochromatosis has repeatedly demonstrated its significance. Medical symptoms of hemochromatosis are prevented or treated by repeated phlebotomy to extract extra iron from the body. Although an improvement of iron consumption in individuals with hemochromatosis seems contraindicated, iron fortification or the usage of the iron supplementation protocol has not been shown to be linked to the risks of hemochromatosis during pregnancy for clinical disease. Even if their iron consumption is about normal, hemochromatosis persons with excess of iron need phlebotomy to minimize iron storage in their body (Services, 1998) .

6.2 Adverse effects after different medications to treat iron deficiency

Adverse effects caused by oral iron supplements:

1. Intestinal habit changes: Constipation is a common side effect of iron additives for anemia, but diarrhea can often occur.

2. Stomach upset: The iron replacement may also develop side effects of stomach pain, bloating, nausea and vomiting.

3. Dark stools

4. Teeth stunned.

5. In the mouth, there is a metallic taste.

6. Heartburn

Source: Adapted from, (*Iron Supplement Side Effects | Iron Deficiency Anemia Treatment*, 2013)

Adverse effects caused by intravenous iron intake:

IV iron has marginal side effects but may include (*Intravenous Iron Infusion*, n.d.):

1. Head, limbs, paws, legs or feet floating or swelling

2. Fatigue, weakness or lightness unexpectedly as you get up from a seat lying or sitting

3. Bowel discomfort, like nausea and cramps

4. Respiratory problems

5. Problems with skin, like rash

6. Low pressure in the blood

Source: Adapted from, (*Intravenous Iron Infusion*, 2016)

6.3 Risk factors

Although anyone may experience iron deficiency anemia, there is a greater chance in some individuals. The doctor will inform the patient if his/her chances of being anemic are at risk (Stoffel et al., 2017). Any factors that raise the iron deficiency anemia risk include:

1. Females of different ages

2. Pregnant women

3. Frequent blood donors

4. Vegetarian people.

6. People ages 65 or older.

Source: Adapted from, (Stoffel et al., 2017).

Chapter 7: Recommendation and guidelines to control Iron deficiency in women

Young girls and non-pregnant women of a childbearing age affecting with iron deficiency which can be prevented by nutritional intake. In the Nutrition and the Health: Dietary Guidelines, information regarding safe diets, including good sources of iron, is accessible. The secondary preventive methods are screening, diagnosis and treatment of iron-deficiency anemia. Duration of screening can use age-specific anemia guidelines (Services, 1998) .

In addition, iron consumption and iron supplements are used as part of primary treatment of iron deficiency during pregnancy. In the Dietary Guidelines, Nutrition and Your Wellbeing contains information about balanced foods, including good sources of iron. Further guidance on women who are pregnant can be contained in the Guide to implementing nutrition through pregnancy and lactation. Screening, diagnosis and treatment of iron anemia was part of the secondary preventive (Services, 1998) .

An Hb concentration or an Hct test can be used to screen women who are at risk for anemia for 4–6 weeks after postpartum. The non-pregnant women's anemia criteria should be included. Risk factors include continuing anemia in the third quarter, severe blood loss during delivery. Postpartum female iron deficiency anemia treatment and follow-up was identical to those of non-pregnant females (Services, 1998). Primary health professionals can help to avoid iron deficiency and monitor it through providing advice before and beyond pregnancy and childbirth to individuals and communities on sound iron nutrition, and the treatment and follow-up to persons with presumptive iron deficiency throughout pregnancy by examining people based on their likelihood of iron deficiency and by providing support. These guidelines would help to minimize iron deficiency symptoms (e.g. premature pregnancies, low birth weight, child-related delays) and thereby boost public health (Services, 1998)

7.1 Prevention of iron deficiency

Primary prevention

Primary iron deficiency prevention ensures that iron consumption is sufficient. For any baby and child's growth and development, it is important to provide a safe supply of dietary iron, as fast growth and low dietary iron will prevent the child from exhausting iron reserves by 4-6 months of age. For children aged less than 2 years, the primary prevention of iron deficiency is the most significant because of the highest risk of iron deficiency across all ages induced by insufficient iron intake. The sufficiency of iron in the nutrition of a baby is a significant determinant of iron in young children's status, as seen by decreases in iron-deficiency anemia that match changes in the feeding of children. Iron deficiency may lead to developmental and behavioral disruptions in infants and young children. There is less proof of the efficacy of primary prevention in pregnant women. Although iron-deficiency anemia is correlated with pre-term baby delivery, well planned control testing of universal iron supplementation is essential in order to evaluate the efficacy of reducing adverse birth results. Iron supplements during pregnancy have been shown to reduce the incidence of iron deficiency anemia (Services, 1998) .

Secondary prevention

Secondary prevention includes iron deficiency screening, diagnosis and treatment. Tests can be conducted for anemia or for earlier iron deficiency markers (e.g., erythrocyte protoporphyrin concentration or serum ferritin concentration). The expense of tests other than Hb concentration and Hct, viability and variability currently preclude their usage in screening. In this population, it should be dependent on the occurrence of iron deficiency in the decision to test a whole population or just those at documented risk for iron deficiency (Services, 1998) .

7.2 Suggestion for the patients

People with iron deficiency anemia are more likely to develop it again, depending on when it started. For example, people who have been operated on weight reduction can also require iron supplements to keep the iron stores in the body. Additional iron is also used in pregnant women's maternal multivitamins. Iron supplements and iron-containing multivitamins cannot be consumed without a health professional consultation, though, since there are so many complications with iron in the body (*Patient education: Anemia caused by low iron in adults (Beyond the Basics) - UpToDate*, 2016)

Finding an iron deficiency, which could be a symptom of some severe disease, such as bowel cancer or other gastrointestinal condition, may often conflict with a health provider's ability to detect iron deficiency. Most men and women do not require additional iron unless they have an underlying disease which decreases the absorption of iron or causes bleeding (Coad & Conlon, 2011b).

Chapter 8: Conclusion & Future Direction

While several of the components of iron metabolism are elucidated, iron deficiency remains one of the world's most frequent nutrient issues. There is emerging evidence that iron depletion can influence neurocognitive activity, including in adults who are unable to compromise their erythropoiesis. This implies that it is important not merely to track the results of iron degradation but to detect early negative iron balance and to decide the proper timing and evaluation of the therapies by selecting the biomarker for the identification of early stages of iron deficiency. After being diagnosed with iron deficiency, different age groups of women need different types of medication which need to be addressed. There has been a decrease in the incidence of iron deficiency in Bangladeshi women, but it is still not sufficient. There needs to be a greater awareness of iron deficiency among patients, particularly in women, and more detailed interventional research should be carried out. It's also necessary to discuss the overview of iron deficiency in women in Bangladesh to evaluate the scenario for future study and scope.

The iron compounds presently offered are inexpensive and readily available but represent a non-physiological iron solution leading to important side effects. As a consequence, iron deficiency and IDA remain untreated, particularly in people with heavy infectious disease burdens. In order for this to be eliminated in the future,

- It is necessary to look past the tactics utilized thus far and try to integrate group interaction with cognitive research methods to optimize supplementation and fortification programs.

- One of the major breakthroughs in this field is that of a new peptide hormone, hepcidin, created in 2001. The research offers a vital insight into iron deficiency amid sufficient intakes, and no obvious bleeding failure in patients with inflammatory diseases.
- And even though historically inadequate parenteral iron treatment was dangerous and ineffective, modern intravenous iron formulations resolve the dangers of anaphylactic and anaphylactic reactions of the previously used dextran portion. Complete iron filling will now be carried out in a day-case outpatient facility.
- Researchers are also beginning to consider more complex aspects of iron deficiency, including the significant consequences of even sub-clinical iron deficiency, before the emergence of Anemia on cardiac and respiratory activity, with these strong medicinal methods.

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